Re: Draft Interim Guidance on Financial Relationships

Dear Ms. Gottfried:

The University of New Mexico (UNM) submits these comments in response to OHRP's proposed Interim Guidance On Financial Relationships in Clinical Research: Issues for Institutions, Clinical Investigators, and IRBs to Consider When Dealing with Issues of Financial Interests and Human Subject Protection (hereafter referred to as Guidance). UNM agrees that little policy guidance now exists for IRBs on this subject but we are concerned that this Guidance from OHRP may not be an appropriate way to provide assistance to institutions. While labeled a "Guidance" the language used is not completely devoid of being prescriptive. If any aspect of the Guidance imposes requirements on institutions such that a failure to comply would expose the institution to any sanction whatsoever, including an adverse finding in a federal agency audit, then this Guidance should be issued as a rulemaking pursuant to the Administrative Procedures Act. If OHRP decides to proceed with issuing this document in its current form, we request that OHRP clarify that the Guidance is voluntary in all respects and an institution's failure to adopt any recommended practice would not subject it to sanction or penalty of any kind.

Issued as a Guidance, institutions will have to determine what course of action to choose when the Guidance uses language that differs from federal rules on the same subject. One concern is the membership of the IRB.

The Guidance at Section 1.3 provides that "broad participation of members from outside the institution" is necessary to protect the integrity of the IRB process. Federal regulations governing IRB membership require at least one member who is not affiliated with the institution. 45 C.F.R. Sec. 46.107.

"Broad participation" certainly suggests that more than one or two outside member is needed. Thus, the Guidance adopts a standard different from federal regulations. Institutions with an approved assurance that includes only one or two non-affiliated IRB members will need to determine what impact the Guidance has on its operations. If OHRP wants to amend federal requirements that must be done through formal rulemaking and not in a policy Guidance.

A number of issues are unclear in the Guidance. The title uses the terms "clinical research" and "clinical investigators" but it is unclear whether this Guidance applies only to IRB consideration of clinical research or to all IRBs. Some provisions, such as, for example, Section 1.2 are limited to clinical research. However, most provisions are not on their face limited to clinical research. For example, Sections 1.3 and 1.4 appear to apply to all IRBs whether or not they review clinical research. One of UNM's institutional review boards reviews only non-medical protocols principally from the social sciences and education. Clinical research is not being conducted under these protocols. The Guidance is unclear on the extent to which it applies to this IRB.

Implementing Section 1.4 would be very difficult since it is unknown in the abstract which entities will be sponsors of research in any given year. Does Section 1.4 mean that IRB staff and members must disclose financial interests only in entities that already sponsor research at the institution? Or must interests be disclosed in entities likely to sponsor research or those that might conceivably sponsor research? Or does this in reality require all IRB staff and members to disclose all financial interests annually? UNM urges OHRP to recognize that institutions rely upon the voluntary participation of faculty and community individuals to serve as IRB members. Imposing onerous and personally invasive disclosure requirements will make it more difficult to recruit and retain excellent IRB members.

Section 2.2 is unclear as to whether the institution's conflict of interest committee must conduct a general transactional review of the fact of the agreement or must review the actual contractual documents.

Clarification is requested regarding Section 3.1. For protocols reviewed on an expedited basis, must a record be kept establishing that the individual IRB member conducting the expedited review did not have a conflict of interest?

Section 4.4 suggests that if a conflict exists the only successful management device is limiting investigator participation in portions of the trial. Yet the PHS regulations on Objectivity in Research, at 42 CFR Part 50, Section 50.605, provide that conflicts of interest may be managed by, for example, disclosure and monitoring. Disqualifying the investigator from

participating in parts of the research is appropriate if other less restrictive measures are insufficient to manage, reduce or eliminate the conflict affecting the objectivity of the research. UNM suggests that Section. 4.4 be revised accordingly to be consistent with 42 CFR Section 50.605.

Section 5.3 requires that the consent document include an explanation of any financial conflict of interest, how it is being managed and what additional protections have been put in place. UNM suggests a modification providing that the consent document be modified "as appropriate" with the IRB deciding on a case-by-case basis what information must be included in the consent document in order to protect research subjects. A blanket requirement that the consent document include everything contained in Section 5.3 will in some situations result in a consent document that is confusing for subjects and unnecessarily elaborate. For example, an institution's conflict of interest committee may find that an investigator who is conducting a clinical trial for a company and who is also a speaker for that company has a potential conflict of interest. The institution's management solution may be a combination of tools such as disclosure and monitoring. Explaining in the consent document why the situation is a conflict, or potential conflict of interest, and how the management tools address the problem could complicate the consent document without really assisting the reader in deciding whether or not to participate in the trial. The IRB should be able to exercise in expertise in determining when and how to modify a consent document because of a financial conflict of interest.

The University of New Mexico appreciates OHRP's consideration of our comments.

Sincerely,

/signed/
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